

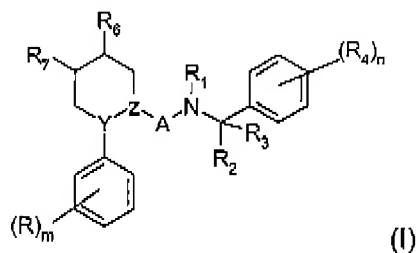
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In the Claims:

Please cancel claims 22-26. Please amend claims 1, 10, 11, 17, 21, 27, 28, 29, 30, 31, 33, 34, 35, 38, 39, 41, 42, 48, 56, 58, 59, 60, 62, 64, 69 and 74 as follows.

Please add new claims 78-80.

1. (Currently Amended) A compound of formula (I)



wherein

R is halogen or C₁₋₄ alkyl;

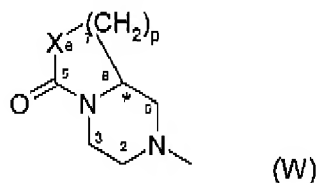
R₁ is C₁₋₄ alkyl;

R₂ or R₃ independently are hydrogen or C₁₋₄ alkyl;

R₄ is trifluoromethyl, C₁₋₄ alkyl, C₁₋₄ alkoxy, trifluoromethoxy or halogen;

R₅ represents hydrogen, C₁₋₄ alkyl or C₃₋₇ cycloalkyl;

R₆ is hydrogen and R₇ is a radical of formula (W):



or R₆ is a radical of formula (W) and R₇ is hydrogen;

X is CH₂, NR₅ or O;

Y is Nitrogen and Z is CH or Y is CH and Z is Nitrogen;

A is C(O) or S(O)_q, provided that when Y is nitrogen and Z is CH, A is not S(O)_q;

m is zero or an integer from 1 to 3;

n is an integer from 1 to 3;

p and q are independently an integer from 1 to 2;

* represents a chiral center;

or a pharmaceutically acceptable salt or ~~solvent~~ hydrate thereof.

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2. (Previously Presented) A compound as claimed in claim 1 R_6 is hydrogen, R_7 is a radical of formula (W) and Y is CH and Z is nitrogen.
3. (Previously Presented) A compound as claimed in claim 1 wherein A is C(O).
4. (Previously Presented) A compound as claimed in claim 1 wherein X is CH_2 .
5. (Previously Presented) A compound as claimed in claim 1 wherein p is 1.
6. (Previously Presented) A compound as claimed in claim 1 wherein each R_4 is independently trifluoromethyl group or halogen and n is 2.
7. (Previously Presented) A compound as claimed in claim 1 wherein each R is independently a halogen or a C_{1-4} alkyl group, wherein m is 0, 1 or 2.
8. (Previously Presented) A compound as claimed in claim 1 wherein R_6 is hydrogen, R_7 is a radical of formula (W) and Y is CH and Z is nitrogen.
9. (Previously Presented) A compound as claimed in claim 1 wherein R_6 is hydrogen, R_7 is a radical of formula (W) and Y is CH and Z is nitrogen.
10. (Currently Amended) A compound selected from :
2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-(6-oxo-hexahydro-pyrrolo[1,2-a]-pyrazin-2-yl)-piperidine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methylamide;
2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-(6-oxo-hexahydro-pyrrolo[1,2-a]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methylamide;
1-(4-Fluoro-2-methyl-phenyl)-4-(6-oxo-hexahydro-pyrrolo[1,2-a]pyrazin-2-yl)-piperidine-2-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
and enantiomers, diastereoisomers, and pharmaceutically acceptable salts or hydrates solvates thereof.
11. (Currently Amended) A compound selected from :

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2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-((8aS)-6-oxo-hexahydro-pyrrolo[1,2-a]-pyrazin-2-yl)-piperidine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methylamide;

2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-((8aR)-6-oxo-hexahydro-pyrrolo[1,2-a]-pyrazin-2-yl)-piperidine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methylamide;

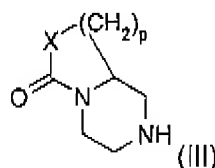
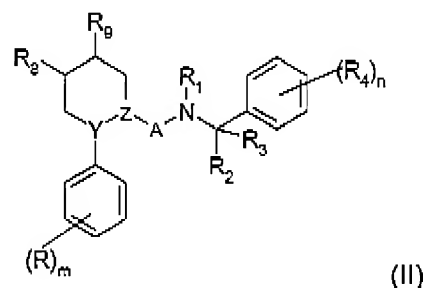
and amorphous and crystalline forms thereof and pharmaceutically acceptable salts or hydrates ~~solvates~~ thereof.

12-14. (Cancelled)

15. (Previously Presented) A pharmaceutical composition comprising a compound as claimed in claim 1 in admixture with one or more pharmaceutically acceptable carriers or excipients.

16. (Canceled)

17. (Currently Amended) A process for the preparation of a compound as claimed in claim 1 comprising reacting a compound of formula (II) wherein R_8 is =O and R_9 is hydrogen or R_8 is hydrogen and R_9 is =O



with compound of formula (III) or a salt thereof in the presence of a suitable metal reducing agent to prepare a compound of formula (I), followed where necessary or desired by one or more of the following steps:

i) removal of any protecting group;

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- ii) isolation of the compound of formula (I) as a salt or a hydrate solvate thereof;
iii) separation of a compound of formula (I) or ~~derivative~~ salt or hydrate thereof into the enantiomers thereof.

18. (Previously Presented) A compound as claimed in claim 1 wherein R_6 is a radical of formula (W), R_7 is a hydrogen and Y is nitrogen and Z is CH.

19. (Previously Presented) A compound as claimed in claim 1 wherein R_6 is a radical of formula (W), R_7 is a hydrogen and Y is nitrogen and Z is CH; A is C(O) and X is CH_2 .

20. (Previously Presented) A compound as claimed in claim 1 wherein R_6 is a radical of formula (W), R_7 is a hydrogen, Y is nitrogen, Z is CH, A is C(O), X is CH_2 , R is independently a halogen or a C_{1-4} alkyl group, R_4 is a trifluoromethyl group, m is 1 or 2, n is 2 and p is 1.

21. (Currently Amended) 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-(6-oxo-hexahydro-pyrrolo[1,2-a]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methylamide and enantiomers, diastereoisomers, and pharmaceutically acceptable salts or ~~solvates~~ hydrates thereof.

22-26. (Canceled.)

27. (Currently Amended) The A method for the treatment of a depressive state or anxiety in man, comprising administering an effective amount of a compound according to claim 1-26, wherein said CNS disorder is selected from depressive states and anxiety.

28. (Currently Amended) The method according to claim 27, wherein said depressive state is selected from
bipolar depression,
unipolar depression,
single or recurrent major depressive episodes,
recurrent brief depression with or without psychotic features, catatonic features,
melancholic features, weight loss, atypical features,

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anxious depression,
cyclothymic or postpartum onset,
dysthymic disorder with early or late onset and with or without atypical features;
neurotic depression;
post traumatic stress disorders;
social phobia;
dementia of the Alzheimer's type, with early or late onset, with depressed mood;
vascular dementia with depressed mood;
mood disorders induced by alcohol, amphetamines, cocaine, hallucinogens,
inhalants, opioids, phencyclidine, sedatives, hypnotics, and ~~anxiolytics and~~
~~other substances~~;
schizoaffective disorder of the depressed type;
adjustment disorder with depressed mood; and
major depressive disorders resulting from a general medical condition.

29. (Currently Amended) The method as claimed in claim 27 ~~26~~, wherein said anxiety is an anxiety disorder ~~CNS disorder is~~ selected from
panic disorders with or without agoraphobia,
agoraphobia,
phobias,
obsessive-compulsive disorder,
post-traumatic stress disorders,
generalized anxiety disorders,
acute stress disorders, and
mixed anxiety-depression disorders.

30. (Currently Amended) The method as claimed in claim 27 ~~26~~, wherein said compound is
2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-(6-oxo-hexahydro-pyrrolo[1,2-a]-pyrazin-2-yl)-
piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-
methylamide;
~~and enantiomers, diastereoisomers, and pharmaceutically acceptable salts or~~
solvates or an enantiomer, diastereoisomer or pharmaceutically acceptable salt or
hydrate thereof.

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31. (Currently Amended) The method as claimed in claim 27 ~~26~~, further comprising administering an effective amount of a serotonin reuptake inhibitor.
32. (Previously Presented) The method as claimed in claim 31, wherein said serotonin reuptake inhibitor is selected from fluoxetine, citalopram, femoxetine, fluvoxamine, paroxetine, indalpine, sertraline and zimeldine.
33. (Currently Amended) The method as claimed in claim 27 ~~26~~, further comprising administering an effective amount of a dopaminergic antidepressant.
34. (Currently Amended) The method as claimed in claim 33, wherein said dopaminergic antidepressant is selected from bupropion ~~bupropion~~ and amineptine.
35. (Currently Amended) A method for the treatment of a major depressive disorder in man comprising administering an effective amount of 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-(6-oxo-hexahydro-pyrrolo[1,2-a]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methylamide, or an enantiomer, diastereoisomer, or pharmaceutically acceptable salt or hydrate ~~solvate~~ thereof.
36. (Previously Presented) The method as claimed in claim 35, wherein said major depressive disorder is selected from bipolar depression and unipolar depression.
37. (Previously Presented) The method as claimed in claim 35, further comprising administering an effective amount of a serotonin reuptake inhibitor selected from fluoxetine, citalopram, femoxetine, fluvoxamine, paroxetine, indalpine, sertraline and zimeldine.
38. (Currently Amended) The method as claimed in claim 35, further comprising administering an effective amount of a dopaminergic antidepressant selected from bupropion ~~bupropion~~ and amineptine.
39. (Currently Amended) A method for the treatment of anxiety in man comprising administering an effective amount of 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-

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(S)-(6-oxo-hexahydro-pyrrolo[1,2-a]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methylamide, or an enantiomer, diastereoisomer, or pharmaceutically acceptable salt or hydrate ~~solvate~~ thereof.

40. (Previously Presented) The method as claimed in claim 39, further comprising administering an effective amount of a serotonin reuptake inhibitor selected from fluoxetine, citalopram, femoxetine, fluvoxamine, paroxetine, indalpine, sertraline and zimeldine.

41. (Currently Amended) The method as claimed in claim 39, further comprising administering an effective amount of a dopaminergic antidepressant selected from bupropion ~~bupropion~~ and amineptine.

42. (Currently Amended) A method for the treatment of panic disorder in man comprising administering an effective amount of 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-(6-oxo-hexahydro-pyrrolo[1,2-a]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methylamide, or an enantiomer, diastereoisomer, or pharmaceutically acceptable salt or hydrate ~~solvate~~ thereof.

43. (Previously Presented) A method for the treatment of emesis in a mammal comprising administering an effective amount of a compound as claimed in claim 1.

44. (Previously Presented) The method as claimed in claim 43, wherein said mammal is man.

45. (Previously Presented) The method as claimed in claim 43, wherein said emesis is delayed emesis.

46. (Previously Presented) The method as claimed in claim 43, wherein said emesis is anticipatory emesis.

47. (Previously Presented) The method as claimed in claim 43, wherein said emesis is induced by cancer chemotherapeutic agents.

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48. (Currently Amended) The method as claimed in claim ~~47~~ 43, wherein said cancer chemotherapeutic agent is selected from cyclophosphamide, carmustine, lomustine, chlorambucil, dactinomycin, doxorubicin, mitomycin-C, bleomycin, cytarabine, methotrexate, 5-fluorouracil, etoposide, vinblastine, vincristine, cisplatin, dacarbazine, procarbazine, hydroxyurea ~~hydroxyurea~~ and combinations thereof.

49. (Previously Presented) The method as claimed in claim 43, wherein said emesis is induced by radiation sickness or radiation therapy.

50. (Previously Presented) The method as claimed in claim 43, wherein said emesis is induced by pregnancy.

51. (Previously Presented) The method as claimed in claim 43, wherein said emesis is induced by post-operative sickness.

52. (Previously Presented) The method as claimed in claim 43, wherein said emesis is induced by migraine.

53. (Previously Presented) The method as claimed in claim 43, wherein said emesis is induced by opiod analgesics.

54. (Previously Presented) The method as claimed in claim 43, further comprising administering an effective amount of a 5HT3 antagonist.

55. (Previously Presented) The method as claimed in claim 54, wherein said 5HT3 antagonist is selected from ondansetron, granisetron and metoclopramide.

56. (Currently Amended) The method as claimed in claim 43, wherein said compound is 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-(6-oxo-hexahydro-pyrrolo[1,2-a]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methylamide, ~~and enantiomers, diastereoisomers, and pharmaceutically acceptable salts or solvates or an enantiomer, diastereoisomer or pharmaceutically acceptable salt or hydrate thereof.~~

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57. (Previously Presented) The method as claimed in claim 56, further comprising administering an effective amount of a 5HT3 antagonist selected from ondansetron, granisetron and metoclopramide.

58. (Currently Amended) A method for the treatment of emesis in man comprising administering an effective amount of 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-(6-oxo-hexahydro-pyrrolo[1,2-a]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methanamide, or an enantiomer, diastereoisomer, or pharmaceutically acceptable salt or hydrate ~~solvate~~ thereof.

59. (Currently Amended) A method for the treatment of a sleep disorder ~~disorders~~ in man comprising administering an effective amount of a compound as claimed in claim 1.

60. (Currently Amended) A method for the treatment of dependence on a substance selected from nicotine, alcohol, caffeine, phencyclidine phencyclidine-like compounds, opiates, benzodiazepines, cocaine, sedative drugs, hypnotic ~~ipnotic~~ drugs, amphetamines, dextroamphetamine, methamphetamine ~~amphetamine-related~~ drugs, and combinations thereof; in man, comprising administering an effective amount of a compound as claimed in claim 1.

61. (Previously Presented) The pharmaceutical composition as claimed in claim 15, further comprising a serotonin reuptake inhibitor.

62. (Currently Amended) The pharmaceutical composition as claimed in claim 61 ~~45~~, wherein said serotonin reuptake inhibitor is selected from fluoxetine, citalopram, femoxetine, fluvoxamine, paroxetine, indalpine, sertraline and zimeldine.

63. (Previously Presented) The pharmaceutical composition as claimed in claim 15, further comprising a dopaminergic antidepressant.

64. (Currently Amended) The pharmaceutical composition as claimed in claim 63, wherein said dopaminergic antidepressant is selected from bupropion ~~bupropion~~ and amineptine.

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65. (Previously Presented) The pharmaceutical composition as claimed in claim 15, further comprising a 5HT3 antagonist.
66. (Previously Presented) The pharmaceutical composition as claimed in claim 65, wherein said 5HT3 antagonist is selected from ondansetron, granisetron and metoclopramide.
67. (Previously Presented) 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-((8aS-6-oxo-hexahydro-pyrrolo[1,2-a]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methylamide hydrochloride.
68. (Previously Presented) 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-((8aS-6-oxo-hexahydro-pyrrolo[1,2-a]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methylamide hydrochloride as anhydrous crystalline form.
69. (Currently Amended) The method as claimed in claim 27 26, wherein said compound is 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-((8aS-6-oxo-hexahydro-pyrrolo[1,2-a]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methylamide hydrochloride.
70. (Previously Presented) A method for the treatment of a major depressive disorder in man comprising administering an effective amount of 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-((8aS-6-oxo-hexahydro-pyrrolo[1,2-a]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methylamide hydrochloride.
71. (Previously Presented) A method for the treatment of anxiety in man comprising administering an effective amount of 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-((8aS-6-oxo-hexahydro-pyrrolo[1,2-a]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methylamide hydrochloride.
72. (Previously Presented) A method for the treatment of panic disorder in man comprising administering an effective amount of 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-((8aS-6-oxo-hexahydro-pyrrolo[1,2-a]-pyrazin-2-yl)-piperidine-1-

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carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methanamide hydrochloride.

73. (Previously Presented) 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-((8aR)-6-oxo-hexahydro-pyrrolo[1,2-a]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methanamide hydrochloride.

74. (Currently Amended) The method as claimed in claim 27, wherein said compound is 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-((8aR)-6-oxo-hexahydro-pyrrolo[1,2-a]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methanamide hydrochloride.

75. (Previously Presented) A method for the treatment of a major depressive disorder in man comprising administering an effective amount of 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-((8aR)-6-oxo-hexahydro-pyrrolo[1,2-a]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methanamide hydrochloride.

76. (Previously Presented) A method for the treatment of anxiety in man comprising administering an effective amount of 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-((8aR)-6-oxo-hexahydro-pyrrolo[1,2-a]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methanamide hydrochloride.

77. (Previously Presented) A method for the treatment of panic disorder in man comprising administering an effective amount of 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-((8aR)-6-oxo-hexahydro-pyrrolo[1,2-a]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methanamide hydrochloride.

78. (New) The method as claimed in claim 59, wherein said compound is 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-((6-oxo-hexahydro-pyrrolo[1,2-a]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methanamide, or an enantiomer, diastereoisomer, or pharmaceutically acceptable salt or hydrate thereof.

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79. (New) A method for the treatment of a sleep disorder in man comprising administering an effective amount of 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-((8aS-6-oxo-hexahydro-pyrrolo[1,2-*a*]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methylamide hydrochloride.

80. (New) A method for the treatment of a sleep disorder in man comprising administering an effective amount of 2-(R)-(4-Fluoro-2-methyl-phenyl)-4-(S)-((8aR)-6-oxo-hexahydro-pyrrolo[1,2-*a*]-pyrazin-2-yl)-piperidine-1-carboxylic acid[1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methylamide hydrochloride.